

**TABLE 9**  
**SUSCEPTIBILITY TO ANTIBIOTICS**

**ERYTHROMYCIN**

Species	(n)	Range	MIC <sub>50</sub>	MIC <sub>90</sub>
<i>Bacillus</i> spp.	20	0.03-2	0.25	2
<i>Bacteroides fragilis</i>	97	0.25-16	1	8
<i>Bordetella bronchiseptica</i>	11	4-32	8	32
<i>Bordetella parapertussis</i>	46	0.125-4	0.25	0.25
<i>Bordetella pertussis</i>	32	1-0.5	0.25	0.25
<i>Bordetella pertussis</i>	75	0.125-0.5	0.125	0.125
<i>Borrelia burgdorferi</i>	10	0.03-0.125	0.03	0.06
<i>Branhamella</i> (Moraxella) <i>catarrhalis</i>	20	0.125-0.5	0.25	0.25
<i>Branhamella</i> (Moraxella) <i>catarrhalis</i>	20	0.125-0.5	0.25	1
<i>Branhamella</i> (Moraxella) <i>catarrhalis</i> (non $\beta$ -lactamase producer)	40	0.06-0.5	0.25	0.5
<i>Branhamella</i> (Moraxella) <i>catarrhalis</i> (non $\beta$ -lactamase producer)	13	0.03-0.125	0.06	0.06
<i>Branhamella</i> (Moraxella) <i>catarrhalis</i> (non $\beta$ -lactamase producer)	14	0.06-1	0.125	1
<i>Branhamella</i> (Moraxella) <i>catarrhalis</i> (non $\beta$ -lactamase producer)	16	0.015-1	0.06	0.25
<i>Branhamella</i> (Moraxella) <i>catarrhalis</i> ( $\beta$ -lactamase producer)	47	0.06-1	0.25	0.5
<i>Branhamella</i> (Moraxella) <i>catarrhalis</i> ( $\beta$ -lactamase	58	0.03-0.25	0.125	0.125

Species	(n)	Range	MIC <sub>50</sub>	MIC <sub>90</sub>
producer)				
<i>Branhamella</i> (Moraxella)	160	0.06-8	0.25	0.5
<i>catarrhalis</i> ( $\beta$ -lactamase producer)				
<i>Branhamella</i> (Moraxella)	35	0.03-0.125	0.06	0.06
<i>catarrhalis</i> ( $\beta$ -lactamase producer)				
<i>Campylobacter jejuni</i>	25	0.5-8	1	4
<i>Campylobacter jejuni</i>	16	0.125-4	0.25	2
<i>Campylobacter pylori</i>	56	0.25-16	0.5	1
<i>Campylobacter pylori</i>	13	0.125-0.25	0.125	0.25
<i>Corynebacterium JK</i>	102	0.5-128	128	128
<i>Corynebacterium JK</i>	19	0.125-64	2	64
<i>Enterococcus faecalis</i>	26	1-64	1	4
<i>Enterococcus faecalis</i>	50	0.06-64	4	64
<i>Enterococcus faecalis</i>	86	0.125-64	1	64
<i>Enterococcus faecalis</i>	97	0.125-128	2	128
<i>Enterococcus faecium</i>	14	0.06-64	1	64
<i>Enterococcus</i> spp.	35	0.06-32	2	32
<i>Haemophilus ducreyi</i>	122	?-0.125	0.004	0.06
<i>Haemophilus influenzae</i>	145	0.5-8	2	2
<i>Haemophilus influenzae</i>	97	0.25-16	1	4
<i>Haemophilus influenzae</i>	22	0.125-8	2	4
(non $\beta$ -lactamase producer)				
<i>Haemophilus influenzae</i>	137	0.06-8	4	8
(non $\beta$ -lactamase producer)				
<i>Haemophilus influenzae</i>	46	0.06-8	4	8
( $\beta$ -lactamase producer)				
<i>Haemophilus influenzae</i>	17	0.25-4	2	4
( $\beta$ -lactamase producer)				
<i>Haemophilus influenzae</i>	22	0.25-16	8	16
(penicillin susceptible)				

Species	(n)	Range	MIC <sub>50</sub>	MIC <sub>90</sub>
<i>Haemophilus influenzae</i> (penicillin resistant)	20	8-16	8	16
<i>Haemophilus parainfluenzae</i>	13	0.5-8	2	4
<i>Legionella</i> spp.	23	0.03-0.25	0.125	0.25
<i>Legionella pneumophila</i>	31	0.0075-0.25	0.06	0.125
<i>Legionella pneumophila</i>	48	0.03-2	0.25	0.5
<i>Legionella pneumophila</i>	2 5	0.125-1	0.25	1
<i>Listeria monocytogenes</i>	13	0.5-1	0.5	0.5
<i>Listeria monocytogenes</i>	16	0.125-2	0.25	1
<i>Listeria monocytogenes</i>	65	0.06-32	0.125	32
<i>Mycoplasma hominis</i>	26	128	128	128
<i>Mycoplasma hominis</i>	20	256	256	256
<i>Mycoplasma pneumoniae</i>	10	0.06-8	0.06	0.06
<i>Mycoplasma pneumoniae</i>	14	0.004-0.03	0.004	0.004
<i>Neisseria gonorrhoeae</i>	19	0.0075-8	0.25	1
<i>Neisseria gonorrhoeae</i> (non $\beta$ -lactamase producer)	73	0.015-4	0.25	2
<i>Neisseria gonorrhoeae</i> (non $\beta$ -lactamase producer)	78	0.03-2	0.25	1
<i>Neisseria gonorrhoeae</i> ( $\beta$ -lactamase producer)	12	0.03-4	0.5	2
<i>Neisseria gonorrhoeae</i> ( $\beta$ -lactamase producer)	17	1-4	2	4
<i>Neisseria meningitidis</i>	19	0.5-8	1	8
<i>Nocardia asteroides</i>	78	0.25-8	8	8
<i>Staphylococcus aureus</i>	44	0.125-1	0.125	0.5
<i>Staphylococcus aureus</i>	100	0.25-128	0.5	4
<i>Staphylococcus aureus</i> (penicillin susceptible)	20	0.125-0.5	0.5	0.5
<i>Staphylococcus aureus</i> (penicillin susceptible)	35	0.06-32	0.25	0.5

Species	(n)	Range	MIC <sub>50</sub>	MIC <sub>90</sub>
<i>Staphylococcus aureus</i> (penicillin resistant)	35	0.25-32	0.25	32
<i>Staphylococcus aureus</i> (methicillin susceptible)	28	0.125-1	0.25	0.5
<i>Staphylococcus aureus</i> (methicillin susceptible)	97	0.125-64	0.25	64
<i>Staphylococcus aureus</i> (methicillin susceptible)	20	0.125-1	0.5	0.5
<i>Staphylococcus aureus</i> (methicillin resistant)	17	0.5-128	128	128
<i>Staphylococcus aureus</i> (methicillin resistant)	15	64	64	64
<i>Staphylococcus aureus</i> (methicillin resistant)	20	64	64	64
<i>Staphylococcus aureus</i> (methicillin resistant)	30	0.06-32	32	32
<i>Staphylococcus coagulase f</i>	10	0.125-4	0.25	2
<i>Staphylococcus coagulase f</i>	100	0.125-64	0.25	64
<i>Staphylococcus coagulase f</i> (non $\beta$ -lactamase producer)	12	0.03-8	0.125	0.25
<i>Staphylococcus coagulase f</i> ( $\beta$ -lactamase producer)	38	0.06-16	0.125	4
<i>Staphylococcus epidermidis</i>	50	0.125-64	64	64
<i>Staphylococcus haemolyticus</i>	20	0.125-64	64	64
<i>Staphylococcus hominis</i>	20	0.125-64	64	64
<i>Streptococcus agalactiae</i>	20	0.03-0.25	0.03	0.125
<i>Streptococcus agalactiae</i>	34	0.015-0.06	0.03	0.03
<i>Streptococcus pneumoniae</i>	58	0.03-0.25	0.06	0.125
<i>Streptococcus pneumoniae</i>	91	0.125-4	0.125	0.125
<i>Streptococcus pneumoniae</i>	50	0.015-0.06	0.03	0.03
<i>Streptococcus pneumoniae</i>	16	0.03-0.125	0.06	0.125
<i>Streptococcus pneumoniae</i>	26	0.015-0.25	0.03	0.06

Species	(n)	Range	MIC <sub>50</sub>	MIC <sub>90</sub>
<i>Streptococcus pneumoniae</i>	50	0.03-0.125	0.06	0.06
<i>Streptococcus pyogenes</i>	19	0.03-0.25	0.06	0.125
<i>Streptococcus pyogenes</i>	20	0.03-0.25	0.06	0.125
<i>Streptococcus pyogenes</i>	33	0.015-0.03	0.03	0.03
<i>Streptococcus pyogenes</i>	20	0.06-32	0.125	32
<i>Streptococcus</i> spp.	22	0.015-0.25	0.03	0.06
<i>Streptococcus</i> spp.	107	0.004-2	0.03	1
<i>Ureaplasma urealyticum</i>	28	0.015-256	2	256
<i>Ureaplasma urealyticum</i>	19	8-128	16	32

**LINCOMYCIN**

Species	(n)	Range	MIC <sub>50</sub>	MIC <sub>90</sub>
<i>Mycoplasma hominis</i>	28	0.5-16	2	4
<i>Mycoplasma pneumoniae</i>	11	2-32	8	32
<i>Staphylococcus aureus</i>	100	0.5-512	1	1
<i>Ureaplasma urealyticum</i>	19	64-128	128	128

## EXAMPLES

The following examples are included to demonstrate preferred embodiments of the invention. It should be appreciated by those of skill in the art that the techniques disclosed in the examples which follow represent techniques discovered by the inventor to function well in the practice of the invention, and thus can be considered to constitute preferred modes for its practice. However, those of skill in the art should, in light of the present disclosure, appreciate that many changes can be made in the specific embodiments which are disclosed and still obtain a like or similar result without departing from the spirit and scope of the invention.

### EXAMPLE 1

#### a. BLAST-based searches

Genomic search strategies for human gene discovery were applied to the Genbank NR, HTGS and EST databases using the BLASTp and tBLASTn programs (Altschul *et al.*, 1990) using the NCBI website tools ([ncbi.nlm.nih.gov/BLAST/](http://ncbi.nlm.nih.gov/BLAST/)). Similar approaches were used to query the Celera mouse genome assembly ([celera.com](http://celera.com)). The Initial queries for the search utilized the amino acid sequences for the known human defensins (DEFB1, DEFB2, DEFB3, DEFB4) (Bensch *et al.*, 1995; Schroder *et al.*; Pend *et al.*, 2001; Harder *et al.*, 2001; Garcia *et al.*, 2001) and the EP2/HE2 sequences (Frolich *et al.*, 2000; Hamil *et al.*, 2000) and the known mouse  $\beta$ -defensins (*Defb1*, *Defb2*, *Defb3*, *Defb4*, *Defb5*, *Defb6*) Huttner *et al.*, 1997; Morrison *et al.*, 1999; Bals *et al.*, 1999; Jia *et al.* 2000; Yamaguchi *et al.*, 2001) and Genbank (AF318068).

For each novel  $\beta$ -defensin gene identified using the *hmmsearch* program (described below), additional iterative BLAST searches were performed against the human and mouse databases to identify additional related sequences and search for expressed sequence tags (ESTs) to confirm that the sequences are transcribed.

#### b. Construction of Hidden Markov Models for the six-cysteine $\beta$ -defensin motif

The complementary strategy used to identify  $\beta$ -defensin genes employed a quantitative sequence analysis using the Hidden Markov Model (Eddy, 1998; Sonnhammer and Durbin, 1997; Iseli *et al.*, 1999). For this purpose, the inventors defined core human and mouse  $\beta$ -defensin amino acid sequences containing the six cysteine motif and sorted them according to their scores in Hidden Markov Chain Models (HMMs) trained on *defensin* motifs. Initially, twelve 36-47 amino acid long second exon 6-cysteine motifs derived from human and mouse  $\beta$ -defensin sequences previously localized to chromosomes 8p23-p22 and 8 were defined by manual inspection of full length  $\beta$ -defensin domain sequences. These motifs were aligned using

the ClustalW program (Thomspon *et al.*, 1990) and trimmed of extra amino acids extending on both sides of a 33-35 amino acid core. These 12 aligned sequences were used as input for the HMMER 2.1.1 suite software (Eddy, 1998) to build the first of our HMM  $\beta$ -defensin models. The program *hmmbuild* was used to construct this first model, and *hmmcalibrate* was used to  
5 calibrate E-value scores. HMMs are well-suited to this task because the scores calculated, once calibrated on the size of the data set, are directly related to the probability that the motif under consideration did not occur by chance. Furthermore, the HMM technique is more flexible and allows uncovering motif occurrences not contained in the initial training set. An optimal HMM may therefore be constructed by an iterative cycle of training and searching cycles, exploring  
10 most of the motif space.

**c. Assembly of human and mouse  $\beta$ -defensin genomic clusters**

To generate continuous DNA sequence for some analyses, the sequences from the human and mouse defensin containing BAC clones and genomic contigs, sequences were aligned using the Sequencher program (Gene Codes Corporation, Ann Arbor, MI).

**d. Analysis of predicted  $\beta$ -defensin peptide sequences: alignment and phylogeny**

The multiple sequence alignment and dendogram construction were performed using the program Pileup from the Wisconsin Package software (Accelrys, San Diego, CA). The amino acid sequences were predicted from the known, related and predicted  $\beta$ -defensin genes in human  
20 and/or mouse and included two residues before and after the six-cysteine domain. The comparison matrix was set at Blosom62 with a gap creation penalty of 8 and a gap extension penalty of 2.

**EXAMPLE 2**

A Hidden Markov Model (HMM) (Sonnhammer *et al.*, 1997; Eddy *et al.*, 1998) was  
25 constructed with the mature peptide sequences predicted from the five known human  $\beta$ -defensin genes (Bensch *et al.*, 1995; Schroder *et al.*, 1999; Harder *et al.*, 2001; Jia *et al.*, 2001; Garcia *et al.*, 2001; Frohlich *et al.*, 2000) and six mouse  $\beta$ -defensin genes (Huttner *et al.*, 1997; Morrison *et al.*, 1999; Bals *et al.*, 1999; Jia *et al.*, 2000; Yamaguchi *et al.*, 2001) (Genbank AF318068). The program *hmmsearch* ([hmm.wustl.edu/](http://hmm.wustl.edu/)) used this HMM to screen about 4 Mb of genomic  
30 DNA sequence around the known  $\beta$ -defensin locus on human chromosome 8p23-p22. Twelve genes were found, including the five known  $\beta$ -defensin genes, DEFB1-4, and HE2/EP2, and six novel genes, DEFB4-8 and DEFBp1 (FIG. 1). When the novel sequences were used for BLAST

analysis of the human genome sequence, another  $\beta$ -defensin gene was found, DEFB10. The HMM was reseeded with the predicted peptide sequence from the new genes and used to analyze the genomic DNA sequence around DEFB10. Four more  $\beta$ -defensin genes, DEFB11-14, were revealed (FIG. 1). Prior to this study, all human defensin genes mapped to chromosome 8p23-p22 (Liu *et al.*, 1997; Bevins *et al.*, 1996; Harder *et al.*, 1997). Surprisingly, the DEFB10-14 genes are located on chromosome 6p12, indicating a second  $\beta$ -defensin gene cluster in the human genome. The BLAST/*hmmsearch* process was iterated and 15 new  $\beta$ -defensins, DEFB15-29, were found (FIG. 1). These genes are located on two sequence contigs that map to chromosome 20q11.1 and 20p13 and represent two more  $\beta$ -defensin gene clusters.

Finally, the 31 human  $\beta$ -defensin genes were combined in a HMM and used to analyze the six-frame translation of the entire human genome with *hmmsearch*. Two new  $\beta$ -defensin genes, DEFB30 and DEFB31, were identified on the same BAC clones and represent a fifth cluster in the human genome. These genes have not been unambiguously mapped and may be located on chromosomes 2, 4, 8 or 11 (FIG. 1). Significantly, only 13 of 31 of the previously identified  $\beta$ -defensin genes were detected, demonstrating that, like BLAST searches, the genome-wide searches with *hmmsearch* alone are not sufficient for identifying all  $\beta$ -defensin genes. Further BLAST and *hmmsearch* analyses did not detect additional sequences in the human genome. In total, 28 novel  $\beta$ -defensin genes were identified in the human genome in five clusters. The predicted partial peptide sequences for these genes are shown in FIG. 1, and the Genbank accession numbers for their genomic sequence is in Appendix 1.

To search for novel  $\beta$ -defensin genes in the mouse genome, a similar approach was used to screen the mouse genome assembly in the Celera database (.celera.com). A total of 39 new sequences were found (Appendix 1) clustered on four chromosomes, 8, 1, 2 and 14. These regions of the mouse genome are syntenic to the human  $\beta$ -defensin clusters at 8p23-p22, 6p12, 20p11, 20q13 and 8p23-p22 (.ncbi.nlm.nih.gov/homology). In addition, many of the predicted gene products from each human cluster were most similar to a predicted gene product located in the syntenic cluster in mouse suggesting that these genes represent homologs (FIG. 2 and Appendix 1). Finally, the order and orientation of the homologs appears to be conserved (FIG. 3). The main exceptions are the homologs between human chromosome 20 and mouse chromosome 2 where one or both clusters appears to have undergone a chromosomal rearrangement. Given the strong synteny between these five loci in the human genome and four loci in the mouse, the inventors conclude that each, individual,  $\beta$ -defensin gene cluster and its syntenic partner originated from a common ancestral gene cluster (Jia *et al.*, 2000; Liu *et al.*, 1997).

To test whether these predicted genes are transcribed, the predicted amino acid sequence for each gene was queried against the six-frame translation of the expressed sequence tag database (dbEST) using tBLASTn. Sequence identity was found in dbEST for 13 human and 10 mouse predicted genes (Appendix 1). ESTs were found for at least one gene from each cluster, except for those from human 6p12/mouse 1. However, preliminary PCR expression studies using a commercially-available cDNA panel showed that all of the hypothetical genes from human 6p12 are expressed in placenta (data not shown). It is not surprising that many of the novel  $\beta$ -defensin genes are not represented in the EST database. For example, the known  $\beta$ -defensin gene DEFB3 is not found in the EST database. This gene is expressed at very low levels in normal tissues, but is induced in response to inflammatory stimuli (Harder *et al.*, Jia *et al.*, 2001; Duits *et al.*, 2001). These preliminary expression studies together with the conservation of the four sequence clusters suggest that many of the 27 human and 39 mouse novel  $\beta$ -defensin genes are expressed and prove that the iterative BLAST/hmmsearch method is an effective approach for gene discovery.

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All of the compositions and methods disclosed and claimed herein can be made and executed without undue experimentation in light of the present disclosure. While the compositions and methods of this invention have been described in terms of preferred embodiments, it will be apparent to those of skill in the art that variations may be applied to the compositions and methods and in the steps or in the sequence of steps of the method described herein without departing from the concept, spirit and scope of the invention. More specifically, it will be apparent that certain agents which are both chemically and physiologically related may be substituted for the agents described herein while the same or similar results would be achieved. All such similar substitutes and modifications apparent to those skilled in the art are deemed to be within the spirit, scope and concept of the invention as defined by the appended claims.

Appendix 1. Sequence information for human and mouse  $\beta$ -defensin genes

$\beta$ -defensin Gene	Chromosome	partial amino acid sequence	Accession Numbers <sup>b</sup>		
			Genomic	Celebra	EST
DEFB1	8p23-p22	YNVSSGGQCLYSACPIFTKIQTCTYRGKAKCK	NT_008268.5		AI688359
Defb1	8	YKCLQHGGLRSCPSNTKLQGTCKPDKPCCKS	AL590630	GA_x5J8B7W5T7M	AW226790
Defb7	8	TRCYKFGGCHYNICPGNSREMSNCHPENLRCCKN	AL590619	GA_x5J8B7W5T7M	n.d.
Defb8	8	ARCYKFGGCHYNICPGNSREMSNCHPENLRCCKN	AL590619	GA_x5J8B7W5T7M	AV281472
Defb2	8	DHCHTNGGCVRAICPPSARRPGSCFPEKNPCCKY	AL590619	GA_x5J8B7W5T7M	AV381893
Defb9	8	ERCHKKGGYC-YFCFSSHKKIGSCFPEWPRCCKN	AL590619	GA_x5J8B7W5T7M	BE991400
DEFB3	8p23-p22	YICRVRRGCAVLSCLPKEEQIGKSTGRKCCRR	NT_019483.5		n.d.
Defb14	8	FFCIRIRGGCAVLNCLGKEEQIGRCSNSGRKCCRK	n.d.	GA_x5J8B7W6WMR (#5)	n.d.
Defb10	8	VSCIRNGGIC-QYRCIGLRHKIGTCGSP-FKCKK	n.d.	GA_x5J8B7W6WMR (#6)	BG081036
Defb3	8	VSCIRKGGRCWR-CIGNTRQIGSCGVFLKCCRR	n.d.	GA_x5J8B7W6WMR (#5)	n.d.
Defb15	8	RACYREGGEC-LORCIGLFHKIGTC-NFRFKCKE	n.d.	GA_x5J8B7W6WMR (#6)	n.d.
Defb4	8	ITCMTNGAICWGP-CPTAFRQIGNCGHFKVRCCKI	n.d.	GA_x5J8B7W6WMR (#5)	AV086680
Defb6	8	VTMSYGGSC-QRSCNGSFRLGCHGHPKIRCCRR	n.d.	GA_x5J8B7W6WMR (#5)	n.d.
Defb5	8	VSCMIGGICRYL-CKGNILQNGCGVTSINCCRR	n.d.	GA_x5J8B7W6WMR (#5)	n.d.
DEFB2	8p23-p22	VTCLKSGAICHVPFCPRRYKQIGTGLPGTKCCCK	NT_019483.5		bf08889
DEFB9	8p23-p22	GHCLNLGVCRRDVKVVEDQIGACRRMK-CCRA	NT_019483.5		aw383156
Defb42	14	CVSLQGTCCRRDICKLIEDEIGACRRMK-CCRL	AC090659	GA_x5J8B7W5DQC	n.d.
DEFB30	2/4p/8p/11q	KQCIALKGVCRDKLSTLDDTIGICNEGKK-CCRR	AC068357.2 (chr 8)		n.d.
Defb41	14	KQCISLKGICKDLACTSSDDTIGVNDVKK-CCRK	AC090659	GA_x5J8B7W5DQC	n.d.
Defb38	8	KKCVQRKNACHYFECPLYYSVGTCYKGGKCCQK	n.d.	GA_x5J8B7W6WMR (#5)	n.d.
Defb40	8	IKCLQGNNNCHIQKCPWFLQVSTCYKGGKCCQK	n.d.	GA_x5J8B7W6WMR (#5)	n.d.
Defb39	8	IQCFQKNWTCNTNQCYPFQDEIGTCYDKRGKCCQK	n.d.	GA_x5J8B7W6WMR (#5)	n.d.
Defb37	8	IACIENKDTCLRLKNCPRLHNWVGTCYEGKGCCHK	n.d.	GA_x5J8B7W6WMR (#5)	n.d.
EP2d/HE2b1	8p23-p22	TICRMQQGICRLFFCHSGEKKRDICSDPWNRCVS	NT_019483.5		aa778602
Ep2d	8	TVCLMQQGHCRLEFMCRSGERKGDICSDPWNRCVP	n.d.	GA_x5J8B7W6WMR (#5)	n.d.
DEFB31	2/4p/8p/11q	DECPSEYHCHRLK-CNADEHAIRYCADEFI-CCKL	AC068357.2 (chr 8)		n.d.
Defb43	14	QDCSKHRH-CRMK-CKANEYAVRYCEDWTI-CCRV	AC090659	GA_x5J8B7W5DQC	n.d.
DEFB26 (ESP13.2)	20p13	KKCLNDVGICKKK-CKPEEMHVKNWAMCGKQDCCV	NT_011493.5	GA_x5L2HTTBG3J	AA994981
Defb22	2	KKCANTLGNCRKM-CRDGEKQTEPATSKCPIGKLCCV	n.d.	GA_x5J8B7W3FJ8	n.d.
DEFB29	20p13	RRCLMGLGRCDRH-CNVDEKEIQCKMKK--CCVG	NT_011493.5	GA_x5L2HTTBG3J	AA401404
Defb23	2	KRCLVGFGRCKDS-CLADETQMCHCKAKK--CCIG	n.d.	GA_x5J8B7W3FJ8	BE646673

DEFB15	20q11.1	RRCYGTGRCRK-SCKEIERKKKEGCKHI-CCVP	NT_028392.2	GA_x5L2HTTW9JV	n.d.
Defb28	2	RTCFYGLGKRR-ICRANEKKKKERC-GERTFCCLR	n.d.	GA_x5J8B7W22L0	AV044615
DEFB4	8p23-p22	RICGYGTARCKK-CRSQERYRIGRCNTYA-CCLR	NT_019483.5	GA_x5L2HTTW9JV	n.d.
DEFB16	20q11.1	NPCELYQGMCRNA-CREYEQYLTCPNDQK-CCLK	NT_028392.2	GA_x5J8B7W22L0	AI552035
Defb29	2	IACELYQGLC-RNACQKYEIQYLS-C-PKTRKCCLK	n.d.	GA_x5L2HTTW9JV	AA939044
DEFB19	20q11.1	LRCMNSGICRAS-CKQEQPYLYCRNCQS-CCLO	NT_028392.2	GA_x5J8B7W3FJ8	AV043850
Defb24	2	LQCMNRGFC-RSSCKKSEQAYFCRTFQM-CCLO	n.d.	GA_x5L2HTTBG3J	n.d.
DEFB28	20p13	KKCFNKVTGYCRKKCKVGRYEIGCLSGKL-CCAN	NT_011493.5	GA_x5J8B7W3FJ8	AW045275
Defb20	2	KRCFSNVEGYCRKKCLRLVEISEMGC-LHGKYCC	n.d.	GA_x5L2HTTBG3J	AI694319
DEFB27	20p13	KKCWNVYQGHCRKICRVNEVPEALCENGRYCCLN	NT_011493.5	GA_x5L2HTTBG3J	n.d.
DEFB17	20q11.1	KSCWIIKGHCRCNCKPGEQVKP-CRNGDY-CCIP	NT_028392.2	GA_x5L2HTTW9JV	n.d.
Defb19	2	KACWVLRGHC-RKHCRSGERVKPC-SNGDYCC	n.d.	GA_x5J8B7W3FJ8	n.d.
DEFB18	20q11.1	KKCWNRSGHCRKQ-CKDGEAVKDTCKNLRA-CCIP	NT_028392.2	GA_x5L2HTTW9JV	AA335178
Defb21	2	KRCLKILGHC-RRHCKDGENMDHGC-KYRVCCVP	n.d.	GA_x5J8B7W3FJ8	n.d.
DEFB20	20q11.1	VECWMDGH-CRLL-CKDGEDSIIIRCNRRK-CCVP	NT_028392.2	GA_x5L2HTTW9JV	AW070283
DEFB25	20p13	QKCMQNVGHCRRRCLDTERYILLCRNKL-CCIS	NT_011493.5	GA_x5L2HTTBG3J	AA935636
Defb26	2	KCWKNSLGYCRVRCQEEERYIYLCRNKVS-CCIH	n.d.	GA_x5J8B7W3FJ8	n.d.
DEFB24	20q11.1	KRCWKQGACQY-CTRQETMHLCPDASL-CCLL	NT_028392.2	GA_x5L2HTTW9JV	n.d.
Defb25	2	KRCWNGQAC-RTFCTRQETFMHLCPDASL-CCLL	n.d.	GA_x5J8B7W3FJ8	n.d.
DEFB23	20q11.1	QRCWNLYGKCRYR-CSKKERVVYICINNKM-CCVK	NT_028392.2	GA_x5L2HTTW9JV	AA933749
Defb36	U	QKCNLHGKC-RHCRSKESVYVCTNGKM-CCVK	n.d.	GA_x5L2HTTW9JV	n.d.
Defb27	2	ERCWKSFGVC-RECAKKESYIFCWNGKL-CCVK	n.d.	GA_x5J8B7W3FJ8	AI415386
DEFB22	20q11.1	ETCWNFRGSCRDB-CLKNERVVFCVSGKL-CCLK	NT_028392.2	GA_x5L2HTTW9JV	AI989655
DEFB21	20q11.1	MKWGKSGRCTR-CKESEVYILCKTEAK-CCVD	NT_028392.2	GA_x5L2HTTW9JV	AI476463
Defb30	14	DTCWKLKGIC-RNTCQKEEIVHIFCGIQL-CCLL	AC090659	GA_x5J8B7W5DQC	n.d.
DEFB11	6p21	RECRIGNGQCKNQ-CHENEIRIAYCIRPETHCCLQ	NT_007402.5	GA_x54KREAYBCL	n.d.
Defb17	1	KECKMRGHC-KLQCSEKELRISFCIRPETHCC	n.d.	GA_x5J8B7W3NRM	n.d.
DEFB12	6p21	KSCTAIGGRCKNQ-CDDSEFRISYCARPTHCCVT	NT_007402.5	GA_x54KREAYBCL	n.d.
DEFB14	6p21	DRCTKRYGRCKRD-CLESEKQIDICSLPRKICCTE	NT_007402.5	GA_x54KREAYBCL	n.d.
EP2c	8p23-p22	VDCRRSEGFQCEY-CNYMETQVGYCSKKDACCCLH	NT_019483.5	GA_x54KREAYBCL	n.d.
Ep2c	8	VNCKKSEGGQCEY-CNFMETQVGYCSKKKEPCCLH	n.d.	GA_x5J8B7W6WNR (#5)	AA778602
DEFB10	6p21	ERCEKVRGICKTF-CDDVEYDYGICIKWRSQCCV	NT_007402.5	GA_x54KREAYBCL	n.d.
Defb16	1	ERCEKVRGMC-KTVCDIDEYDYGICIRWRNQCCI	n.d.	GA_x5J8B7W3NRM	n.d.
DEFB13	6p21	KRECQLVRGACKPECNSWEVYVYCNVNF--CCAV	NT_007402.5	GA_x54KREAYBCL	n.d.
Defb18	1	HKCSLVRGTC-KSECNNSWEYKYNIC--HTEPCCVV	n.d.	GA_x5J8B7W3NRM	n.d.
Defb12	8	ETCRLGRGKCRRT-CIESEKIAGWCKLNFF-CCRE	n.d.	GA_x5J8B7W6WNR (#5)	n.d.
Defb35	8	ETCRLGRGKC-RRACIESEKIVGWCKLNFF-CCRE	AL590619	GA_x5J8B7W5T7M	n.d.

DEFB5	8p23-p22	ESCKLGRGKRKE-CLENEKPDGNRLNFL-CCRQ	NT_019483.5	n.d.
DEFB7	8p23-p22	TNCFLYLARTAIHRALISKRMEGHCEAE-CLTFEVKI	NT_019483.5	n.d.
Defb13	8	FICKQWNGQC-EAECFTFEQKIGTC-QANFLCCRK	AL590619	n.d.
Defb11	8	EKCSRVRNGRCTAS-CLKNEELVALC-QKNLKCCVT	AL590619	n.d.
Defb34	8	EKCSRINGRC-TASCLKNEELVALCWKNLK-CCVT	n.d.	n.d.
DEFB6	8p23-p22	EKCNKLGKTCNN-CGKNEELIALCQKSLK-CCRT	NT_019483.5	aw103145
DEFB8	8p23-p22	EICERPNGSCRDF-CLETEIHVGRCLNSRP-CCLP	NT_019483.5	aa406058
Defb32	U	KLCLDQKDTCPDSRTC-LEGTQP-CHPHHPNCCES	n.d.	n.d.
Defb33	U	RPCEKMGGICKSQKTHGCSILPAECKSRYKHCCRL	n.d.	n.d.
Defb31	U	CRSWGTCSTAAICFDSLSRRGQCGPVKDPCCPL	n.d.	BG968591
DEFBp1	8p23-p22	ZRCVCVLNV CSTSLKQIGTYGHDRIKCKK	NT_019483.5	pseudogene
Defbp1	8	LTCIANRGFC-WHSCIQGFQLAGHCGHPKVRLLH	n.d.	pseudogene
Defbp2	8	LVCRRKGGRC-YIKCPDNTDZIGMCLP-FKCKRQ	n.d.	pseudogene
Defbp3	U	LSCWMKZGIC-QYRCFGNTHKIGSCGAPFLKCKR	n.d.	pseudogene

<sup>a</sup> Human genes are capitalized and mouse genes are in italics.

<sup>b</sup> No data (n.d.). Only a single accession number is given for each gene, though others may exist.

**REFERENCES**

The following references, to the extent that they provide exemplary procedural or other details supplementary to those set forth herein, are specifically incorporated herein by reference.

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- 15 U.S. Patent No. 4,879,236  
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**CLAIMS**

1. An isolated antimicrobial peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOS:1-82.
- 5 2. The antimicrobial peptide of claim 1, wherein said antimicrobial peptide is comprised in a pharmaceutically acceptable composition.
3. The antimicrobial peptide of claim 2, wherein said pharmaceutical composition is formulated for topical administration.
- 10 4. The antimicrobial peptide of claim 2, wherein said pharmaceutical composition is formulated for oral administration.
5. The antimicrobial peptide of claim 2, wherein said pharmaceutical composition is formulated for parenteral administration.
- 15 6. The antimicrobial peptide of claim 5, wherein said pharmaceutical composition is formulated for administration by injection.
- 20 7. The antimicrobial peptide of claim 5, wherein said pharmaceutical composition is formulated for administration by inhalation.
8. An isolated nucleic acid molecule encoding a peptide selected from the group consisting of SEQ ID NOS:1-82, said nucleic acid molecule isolated free from other human or murine coding sequences.
- 25 9. The nucleic acid molecule of claim 8, wherein said nucleic acid is incorporated into an expression vector.
- 30 10. A viral vector comprising a nucleic acid molecule encoding a peptide selected from the group consisting of SEQ ID NOS:1-82.

11. The viral vector of claim 10, wherein said viral vector is selected from the group consisting of adenovirus, adeno-associated virus, vaccinia virus, retrovirus, herpesvirus, and polyomavirus.
- 5 12. An isolated nucleic acid molecule encoding a peptide selected from the group consisting of SEQ ID NOS:1-82, and a promoter heterologous to the coding region for said peptide.
13. The isolated nucleic acid molecule of claim 12, wherein said promoter is CMV IE.
- 10 14. The isolated nucleic acid molecule of claim 12, further comprising one or more of an origin of replication, a polyadenylation signal, an internal ribosome entry site, a multipurpose cloning site and a selectable marker.
- 15 15. An isolated nucleic acid molecule encoding a peptide selected from the group consisting of SEQ ID NOS:1-82, said nucleic acid molecule being 10,000 base pair in length or shorter.
16. The isolated nucleic acid molecule of claim 15, said nucleic acid molecule being 5000 base pairs or shorter.
- 20 17. The isolated nucleic acid molecule of claim 15, said nucleic acid molecule being 2500 base pairs or shorter.
18. The isolated nucleic acid molecule of claim 15, said nucleic acid molecule being 1000 base pairs or shorter.
- 25 19. The isolated nucleic acid molecule of claim 15, said nucleic acid molecule being 500 base pairs or shorter.
- 30 20. A method of inhibiting the growth of a microbe comprising introducing into an environment containing said microbe a peptide selected from the group consisting of SEQ ID NOS:1-82.

21. The method of claim 20, wherein said peptide is introduced in a composition capable of sustaining the antimicrobial properties of said peptide in said environment.
22. The method of claim 21, wherein said peptide is delivered in a pharmaceutical composition.
23. The method of claim 20, further comprising introducing an additional antimicrobial agent into said environment.
24. The method of claim 23, wherein said peptide is introduced before said additional antimicrobial agent.
25. The method of claim 23, wherein said peptide and said additional antimicrobial agent are introduced concurrently.
26. The method of claim 23, wherein said peptide is introduced after said additional antimicrobial agent.
27. The method of claim 23, wherein said additional antimicrobial agent is selected from the group consisting of a protein synthesis inhibitor, a cell wall growth inhibitor, a cell membrane synthesis inhibitor, a nucleic acid synthesis inhibitor, and a competitive inhibitor.
28. The method of claim 20, wherein said environment is a surgical field or wound site.
29. A kit comprising an antimicrobial peptide, wherein said peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:1-82, disposed in a suitable container.
30. The kit of claim 29, further comprising an additional antimicrobial agent.
31. A method of inhibiting growth of a microbe in a host, comprising administering to said host a peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOS:1-82.

32. The method of claim 31, further comprising administering an additional antimicrobial agent.
- 5 33. The method of claim 32, wherein said peptide is administered before said additional antimicrobial agent.
34. The method of claim 32, wherein said peptide and said additional antimicrobial agent are administered concurrently.
- 10 35. The method of claim 32, wherein said peptide is administered after said additional antimicrobial agent.
- 15 36. The method of claim 32, wherein said additional antimicrobial agent is selected from the group consisting of a protein synthesis inhibitor, a cell wall growth inhibitor, a cell membrane synthesis inhibitor, a nucleic acid synthesis inhibitor, and a competitive inhibitor.
- 20 37. A medical device coated with one or more peptides selected from the group consisting of SEQ ID NOS:1-82.
38. The medical device of claim 37, wherein said medical device is a catheter, a needle, a sheath, and a stent.
- 25 39. An antimicrobial composition comprising one or more peptides selected from the group consisting of SEQ ID NOS:1-82 and one or more non-peptide antimicrobial agents.
- 30 40. A method of treating a bacterial infection comprising administering to a subject a peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOS:1-82.
41. A method of activating a memory T cell comprising contacting a memory T cell with a peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOS:1-82.

42. A method of activating an immature dendritic cell comprising contacting an immature dendritic cell with a peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOS:1-82.

5

43. A method of stimulating adaptive immune response comprising contacting a subject with a peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOS:1-82.

10

44. A method of inhibiting a multidrug resistant bacterium comprising treating said bacterium with a peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOS:1-82.

15

45. The method of claim 44, further comprising treating said bacterium with an additional antimicrobial agent.

Gene	Chr	Gene class	Amino acid sequence of six-cysteine domain
DEFB01 (ref)	8	K	YNCVS--SGGQCLYSACPIFTKIQTGYR-GKAKCK
DEFB02 (ref)	8	K	VTCLK--SGAICHVPVFCPRRYKQIGTCGL-PGTKCKKKP
DEFB03 (ref)	8	K	YYCRV--RGGRCVLSCLPKEEQIGKCST-RGRKCCRRKK
DEFB04 (ref)	8	K	RICGY--GTARCRKK-CRSQEYRIGRCPN--TYACCLRK
DEFB05	8	P	ESCKL--GRGKCRKE-CLENEKPDGNCRL--NFLCCRQRI
DEFB06	8	R	EKCNK--LKGTCNN-CGKNEELIALCQK--SLKCCRTIQPCGSIID
DEFB07	8	P	TNC (+21) CEAE-CLTFEVKIGGCRAELAPFCCNRRKH
DEFB08	8	P	EICER--PNGSCRDF-CLETEIHVGRCLN--SRPCCPLGHQ+11
DEFB09	8	P	GHCLN--LSGVCRRDVCKVVEDQIGACRR--RMKCCRAWIL+21
EP2c	8	K	VDCRR--SEGFCQY-CNYMETQVGYCSK-KKDACLH
EP2d	8	K	TICRM--QQGICRLFFCHSGEKKRDICSD-PWNRCCVSNDE
DEFB10	6	P	ERCEK--VRGICKTF-CDDVEYDY-YCIK-WRSQCCV
DEFB11	6	P	RECR1--GNGQCKNQ-CHENEIRIAYCIR-PGTHCCLQQ
DEFB12	6	P	KSCTA--IGGRCKNQ-CDDSEFRISYCAR-PTTHCCVTECDP
DEFB13	6	P	RECQL--VRGACKPE-CNSWEYVYYCNV---NPCCAVWE
DEFB14	6	P	DRCTK--RYGRCKRD-CLESEKQIDICSL-PRKICCTEKL
DEFB15	20	P	RRCY--GTGRCKRS-CKEIERKKEKCGE--KHICCVPEKD+16
DEFB16	20	P	NPCEL--YQGMCRNA-CREYEIQYLTCPN--DQKCLKLSVK+28
DEFB17	20	P	KSCWI--IKGHCRKN-CKPGEQVKPKCN--GDYCCIPSNDS
DEFB18	20	R	KKCWN--RSGHCRKQ-CKDGEAVKDTCKN--LRACCIPSNED+62
DEFB19	20	R	LRCMG--NSGICRAS-CKKNEQPYLYCRN--CQSCCLQSYMR+22
DEFB20	20	R	VECWM---DGHCRLL-CKDGEDSIIRCN--RKRCVPSRYL+32
DEFB21	20	R	MKCWG--KSGRCRTT-CKESEVYIILCKT--EAKCCVDPKYV+19
DEFB22	20	R	ETCWN--FRGSCRDE-CLKNERVYVFCVS--GKLCCCLKPKDQ+9
DEFB23	20	R	QRCWN--LYGKCRYR-CSKKERVYVYCIN--NKMCCVKPKYQ+8
DEFB24	20	P	KRCWK--GQGACQTY-CTRQETYMHLCPD--ASLCCLSYALK+10
DEFB25	20	R	QKCWN-NVGHCRRR-CLDTERYIILCRN--KLSCCISIIH+94
DEFB26	20	R	KKCLN--DVGICKKK-CKPEEM(+8) CGK--QRDCCVPADRR+46
DEFB27	20	R	KKCWNNYVQGHCRKI-CRVNEVPEALCEN--GRYCCLNKEL+39
DEFB28	20	P	KKCFN-KVTGYCRKK-CKVGERYEIGCLS--GKLCCANDEEE+34
DEFB29	20	R	RRCLM--GLGRCDH-CNVDEKEIQCKM---KKCCVGPKV+123
DEFB30	4/11/08	P	KQCIA--LKGVCRDKLCSTLDDTIGICNE--GKKCCRRWW
DEFB31	4/11/08	P	DECPS--EYYHCRLK-CNADEHAIRYCAD--FSICCKLKI
Consensus			KKC...GRCK.-CR..E..I..C....KCC

FIG. 1

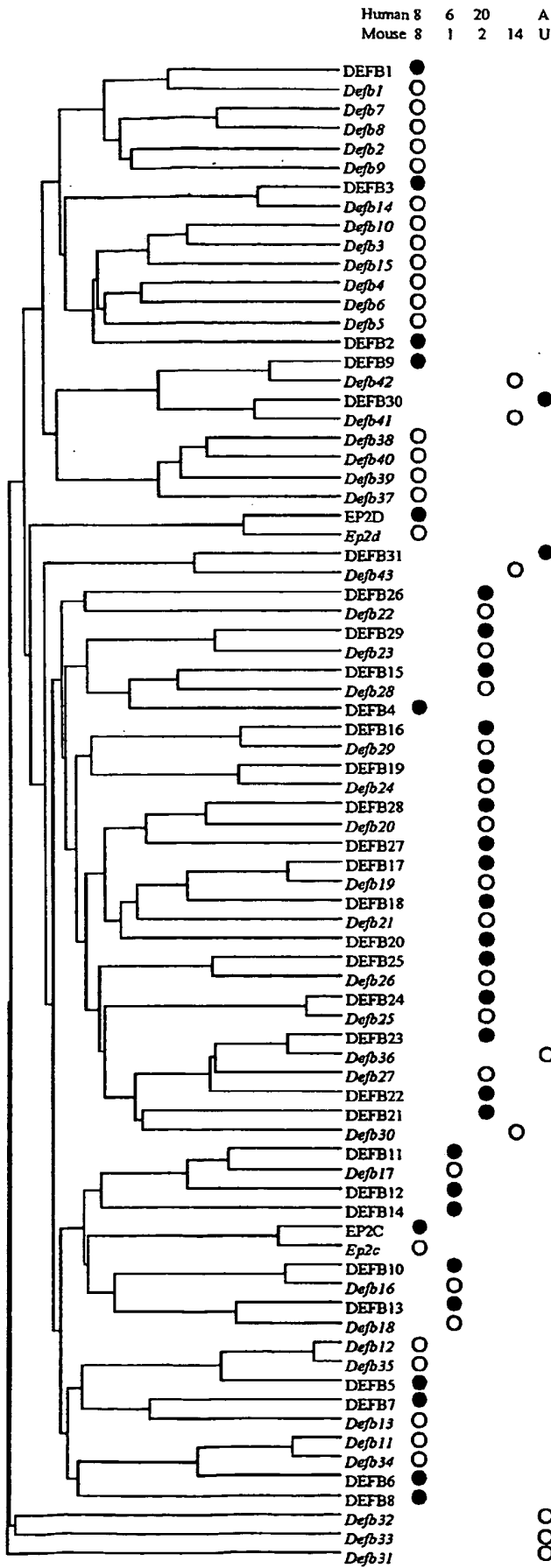


FIG. 2

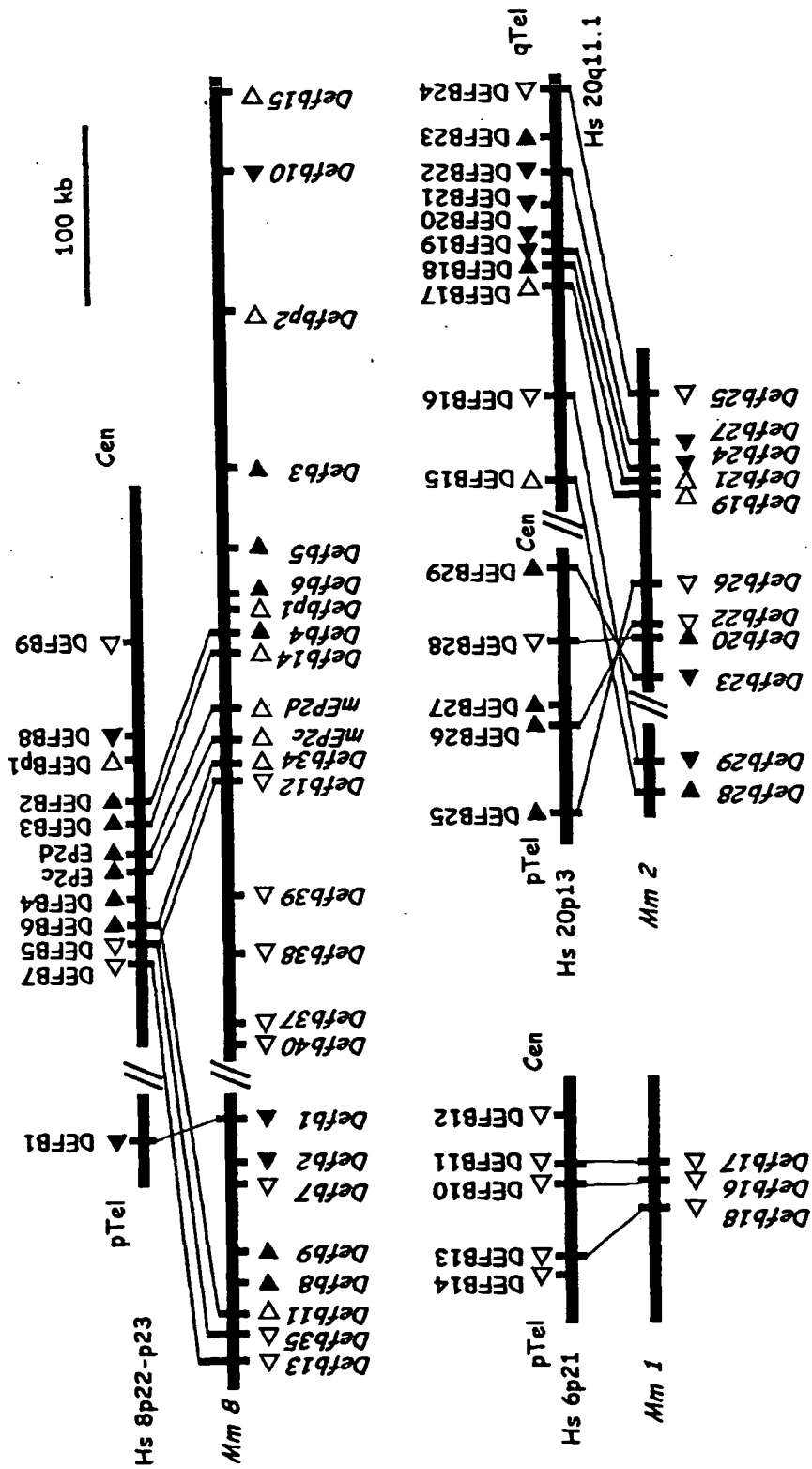


FIG. 3

## SEQUENCE LISTING

&lt;110&gt; UNIVERSITY OF IOWA RESEARCH FOUNDATION

MCCRAY, JR., PAUL B.

SCHUTTE, BRIAN C.

JIA, HONG PENG

CASAVANT, THOMAS L.

<120> HUMAN AND MOUSE  $\beta$ -DEFENSINS, ANTIMICROBIAL PEPTIDES

&lt;130&gt; IOWA:041WO

&lt;140&gt; UNKNOWN

&lt;141&gt; 2002-09-23

&lt;150&gt; 60/323,991

&lt;151&gt; 2001-09-21

&lt;160&gt; 82

&lt;170&gt; PatentIn Ver. 2.1

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Cys Lys

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 <212> PRT  
 <213> Mus musculus

<400> 14  
 Val Ser Cys Cys Met Ile Gly Gly Ile Cys Arg Tyr Leu Cys Lys Gly  
 1 5 10 15  
 Asn Ile Leu Gln Asn Gly Asn Cys Gly Val Thr Ser Leu Asn Cys Cys

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20

25

30

Lys Arg

&lt;210&gt; 15

&lt;211&gt; 35

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 15

Val	Thr	Cys	Leu	Lys	Ser	Gly	Ala	Ile	Cys	His	Pro	Val	Phe	Cys	Pro
1				5					10					15	

Arg	Arg	Tyr	Lys	Gln	Ile	Gly	Thr	Cys	Gly	Leu	Pro	Gly	Thr	Lys	Cys
			20					25						30	

Cys	Lys	Lys
		35

&lt;210&gt; 16

&lt;211&gt; 34

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 16

Gly	His	Cys	Leu	Asn	Leu	Ser	Gly	Val	Cys	Arg	Arg	Asp	Val	Cys	Lys
1				5					10					15	

Val	Val	Glu	Asp	Gln	Ile	Gly	Ala	Cys	Arg	Arg	Arg	Met	Lys	Cys	Cys
			20					25					30		

Arg Ala

&lt;210&gt; 17

&lt;211&gt; 32

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 17

Cys	Val	Ser	Leu	Gln	Gly	Thr	Cys	Arg	Arg	Asp	Ile	Cys	Lys	Leu	Ile
1				5					10					15	

Glu	Asp	Glu	Ile	Gly	Ala	Cys	Arg	Arg	Arg	Trp	Lys	Cys	Cys	Arg	Leu
			20					25					30		

&lt;210&gt; 18

&lt;211&gt; 34

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 18

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Lys Gln Cys Ile Ala Leu Lys Gly Val Cys Arg Asp Lys Leu Cys Ser  
 1 5 10 15

Thr Leu Asp Asp Thr Ile Gly Ile Cys Asn Glu Gly Lys Lys Cys Cys  
 20 25 30

Arg Arg

<210> 19

<211> 34

<212> PRT

<213> Mus musculus

<400> 19

Lys Gln Cys Ile Ser Leu Lys Gly Ile Cys Lys Asp Leu Ala Cys Thr  
 1 5 10 15

Ser Ser Asp Asp Thr Ile Gly Val Cys Asn Asp Val Lys Lys Cys Cys  
 20 25 30

Arg Lys

<210> 20

<211> 35

<212> PRT

<213> Mus musculus

<400> 20

Lys Lys Cys Val Gln Arg Lys Asn Ala Cys His Tyr Phe Glu Cys Pro  
 1 5 10 15

Trp Leu Tyr Tyr Ser Val Gly Thr Cys Tyr Lys Gly Lys Gly Lys Cys  
 20 25 30

Cys Gln Lys  
 35

<210> 21

<211> 35

<212> PRT

<213> Mus musculus

<400> 21

Ile Lys Cys Leu Gln Gly Asn Asn Asn Cys His Ile Gln Lys Cys Pro  
 1 5 10 15

Trp Phe Leu Leu Gln Val Ser Thr Cys Tyr Lys Gly Lys Gly Arg Cys  
 20 25 30

Cys Gln Lys  
 35

<210> 22

<211> 35

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&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 22

Ile Gln Cys Phe Gln Lys Asn Asn Thr Cys His Thr Asn Gln Cys Pro  
 1 5 10 15

Tyr Phe Gln Asp Glu Ile Gly Thr Cys Tyr Asp Lys Arg Gly Lys Cys  
 20 25 30

Cys Gln Lys  
 35

&lt;210&gt; 23

&lt;211&gt; 35

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 23

Ile Ala Cys Ile Glu Asn Lys Asp Thr Cys Arg Leu Lys Asn Cys Pro  
 1 5 10 15

Arg Leu His Asn Val Val Gly Thr Cys Tyr Glu Gly Lys Gly Lys Cys  
 20 25 30

Cys His Lys  
 35

&lt;210&gt; 24

&lt;211&gt; 35

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 24

Thr Ile Cys Arg Met Gln Gln Gly Ile Cys Arg Leu Phe Phe Cys His  
 1 5 10 15

Ser Gly Glu Lys Lys Arg Asp Ile Cys Ser Asp Pro Trp Asn Arg Cys  
 20 25 30

Cys Val Ser  
 35

&lt;210&gt; 25

&lt;211&gt; 35

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 25

Thr Val Cys Leu Met Gln Gln Gly His Cys Arg Leu Phe Met Cys Arg  
 1 5 10 15

Ser Gly Glu Arg Lys Gly Asp Ile Cys Ser Asp Pro Trp Asn Arg Cys  
 20 25 30

Cys Val Pro  
 35

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<210> 26  
 <211> 33  
 <212> PRT  
 <213> Homo sapiens

<400> 26  
 Asp Glu Cys Pro Ser Glu Tyr Tyr His Cys Arg Leu Lys Cys Asn Ala  
     1                    5                    10                    15  
 Asp Glu His Ala Ile Arg Tyr Cys Ala Asp Phe Ser Ile Cys Cys Lys  
             20                    25                    30

Leu

<210> 27  
 <211> 32  
 <212> PRT  
 <213> Mus musculus

<400> 27  
 Gln Asp Cys Ser Lys His Arg His Cys Arg Met Lys Cys Lys Ala Asn  
     1                    5                    10                    15  
 Glu Tyr Ala Val Arg Tyr Cys Glu Asp Trp Thr Ile Cys Cys Arg Val  
             20                    25                    30

<210> 28  
 <211> 37  
 <212> PRT  
 <213> Homo sapiens

<400> 28  
 Lys Lys Cys Leu Asn Asp Val Gly Ile Cys Lys Lys Lys Cys Lys Pro  
     1                    5                    10                    15  
 Glu Glu Met His Val Lys Asn Gly Trp Ala Met Cys Gly Lys Gln Arg  
             20                    25                    30

Asp Cys Cys Val Pro  
             35

<210> 29  
 <211> 37  
 <212> PRT  
 <213> Mus musculus

<400> 29  
 Lys Lys Cys Ala Asn Thr Leu Gly Asn Cys Arg Lys Met Cys Arg Asp  
     1                    5                    10                    15  
 Gly Glu Lys Gln Thr Glu Pro Ala Thr Ser Lys Cys Pro Ile Gly Lys

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20

25

30

Leu Cys Cys Val Leu  
35

&lt;210&gt; 30

&lt;211&gt; 32

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 30

Arg Arg Cys Leu Met Gly Leu Gly Arg Cys Arg Asp His Cys Asn Val  
1 5 10 15

Asp Glu Lys Glu Ile Gln Lys Cys Lys Met Lys Lys Cys Cys Val Gly  
20 25 30

&lt;210&gt; 31

&lt;211&gt; 32

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 31

Lys Arg Cys Leu Val Gly Phe Gly Lys Cys Lys Asp Ser Cys Leu Ala  
1 5 10 15

Asp Glu Thr Gln Met Gln His Cys Lys Ala Lys Lys Cys Cys Ile Gly  
20 25 30

&lt;210&gt; 32

&lt;211&gt; 33

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 32

Arg Arg Cys Tyr Tyr Gly Thr Gly Arg Cys Arg Lys Ser Cys Lys Glu  
1 5 10 15

Ile Glu Arg Lys Lys Glu Lys Cys Gly Glu Lys His Ile Cys Cys Val  
20 25 30

Pro

&lt;210&gt; 33

&lt;211&gt; 33

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 33

25211793.1

Arg Thr Cys Phe Tyr Gly Leu Gly Lys Cys Arg Arg Ile Cys Arg Ala  
 1 5 10 15

Asn Glu Lys Lys Lys Glu Arg Cys Gly Glu Arg Thr Phe Cys Cys Leu  
 20 25 30

Arg

<210> 34  
 <211> 33  
 <212> PRT  
 <213> Homo sapiens

<400> 34  
 Arg Ile Cys Gly Tyr Gly Thr Ala Arg Cys Arg Lys Lys Cys Arg Ser  
 1 5 10 15

Gln Glu Tyr Arg Ile Gly Arg Cys Pro Asn Thr Tyr Ala Cys Cys Leu  
 20 25 30

Arg

<210> 35  
 <211> 33  
 <212> PRT  
 <213> Homo sapiens

<400> 35  
 Asn Pro Cys Glu Leu Tyr Gln Gly Met Cys Arg Asn Ala Cys Arg Glu  
 1 5 10 15

Tyr Glu Ile Gln Tyr Leu Thr Cys Pro Asn Asp Gln Lys Cys Cys Leu  
 20 25 30

Lys

<210> 36  
 <211> 33  
 <212> PRT  
 <213> Mus musculus

<400> 36  
 Ile Ala Cys Glu Leu Tyr Gln Gly Leu Cys Arg Asn Ala Cys Gln Lys  
 1 5 10 15

Tyr Glu Ile Gln Tyr Leu Ser Cys Pro Lys Thr Arg Lys Cys Cys Leu  
 20 25 30

Lys

<210> 37  
 <211> 33  
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&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 37

Leu Arg Cys Met Gly Asn Ser Gly Ile Cys Arg Ala Ser Cys Lys Lys  
 1 5 10 15

Asn Glu Gln Pro Tyr Leu Tyr Cys Arg Asn Cys Gln Ser Cys Cys Leu  
 20 25 30

Gln

&lt;210&gt; 38

&lt;211&gt; 33

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 38

Leu Gln Cys Met Gly Asn Arg Gly Phe Cys Arg Ser Ser Cys Lys Lys  
 1 5 10 15

Ser Glu Gln Ala Tyr Phe Tyr Cys Arg Thr Phe Gln Met Cys Cys Leu  
 20 25 30

Gln

&lt;210&gt; 39

&lt;211&gt; 34

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 39

Lys Lys Cys Phe Asn Lys Val Thr Gly Tyr Cys Arg Lys Lys Cys Lys  
 1 5 10 15

Val Gly Glu Arg Tyr Glu Ile Gly Cys Leu Ser Gly Lys Leu Cys Cys  
 20 25 30

Ala Asn

&lt;210&gt; 40

&lt;211&gt; 32

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 40

Lys Arg Cys Phe Ser Asn Val Glu Gly Tyr Cys Arg Lys Lys Cys Arg  
 1 5 10 15

Leu Val Glu Ile Ser Glu Met Gly Cys Leu His Gly Lys Tyr Cys Cys  
 20 25 30

<210> 41  
 <211> 35  
 <212> PRT  
 <213> Homo sapiens

<400> 41  
 Lys Lys Cys Trp Asn Asn Tyr Val Gln Gly His Cys Arg Lys Ile Cys  
 1 5 10 15  
 Arg Val Asn Glu Val Pro Glu Ala Leu Cys Glu Asn Gly Arg Tyr Cys  
 20 25 30  
 Cys Leu Asn  
 35

<210> 42  
 <211> 33  
 <212> PRT  
 <213> Homo sapiens

<400> 42  
 Lys Ser Cys Trp Ile Ile Lys Gly His Cys Arg Lys Asn Cys Lys Pro  
 1 5 10 15  
 Gly Glu Gln Val Lys Lys Pro Cys Lys Asn Gly Asp Tyr Cys Cys Ile  
 20 25 30  
 Pro

<210> 43  
 <211> 31  
 <212> PRT  
 <213> Mus musculus

<400> 43  
 Lys Ala Cys Trp Val Leu Arg Gly His Cys Arg Lys His Cys Arg Ser  
 1 5 10 15  
 Gly Glu Arg Val Arg Lys Pro Cys Ser Asn Gly Asp Tyr Cys Cys  
 20 25 30

<210> 44  
 <211> 33  
 <212> PRT  
 <213> Homo sapiens

<400> 44  
 Lys Lys Cys Trp Asn Arg Ser Gly His Cys Arg Lys Gln Cys Lys Asp  
 1 5 10 15  
 Gly Glu Ala Val Lys Asp Thr Cys Lys Asn Leu Arg Ala Cys Cys Ile  
 20 25 30  
 Pro

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<210> 45  
 <211> 33  
 <212> PRT  
 <213> Mus musculus

<400> 45  
 Lys Arg Cys Leu Lys Ile Leu Gly His Cys Arg Arg His Cys Lys Asp  
 1 5 10 15  
 Gly Glu Met Asp His Gly Ser Cys Lys Tyr Tyr Arg Val Cys Cys Val  
 20 25 30

Pro

<210> 46  
 <211> 32  
 <212> PRT  
 <213> Homo sapiens

<400> 46  
 Val Glu Cys Trp Met Asp Gly His Cys Arg Leu Leu Cys Lys Asp Gly  
 1 5 10 15  
 Glu Asp Ser Ile Ile Arg Cys Arg Asn Arg Lys Arg Cys Cys Val Pro  
 20 25 30

<210> 47  
 <211> 34  
 <212> PRT  
 <213> Homo sapiens

<400> 47  
 Gln Lys Cys Trp Lys Asn Asn Val Gly His Cys Arg Arg Arg Cys Leu  
 1 5 10 15  
 Asp Thr Glu Arg Tyr Ile Leu Leu Cys Arg Asn Lys Leu Ser Cys Cys  
 20 25 30

Ile Ser

<210> 48  
 <211> 33  
 <212> PRT  
 <213> Mus musculus

<400> 48  
 Lys Cys Trp Lys Asn Ser Leu Gly Tyr Cys Arg Val Arg Cys Gln Glu  
 1 5 10 15

Glu Glu Arg Tyr Ile Tyr Leu Cys Lys Asn Lys Val Ser Cys Cys Ile  
                   20                                  25                                  30

His

<210> 49  
 <211> 33  
 <212> PRT  
 <213> Homo sapiens

<400> 49  
 Lys Arg Cys Trp Lys Gly Gln Gly Ala Cys Gln Thr Tyr Cys Thr Arg  
   1                                  5                                  10                                  15

Gln Glu Thr Tyr Met His Leu Cys Pro Asp Ala Ser Leu Cys Cys Leu  
                   20                                  25                                  30

Ser

<210> 50  
 <211> 33  
 <212> PRT  
 <213> Mus musculus

<400> 50  
 Lys Arg Cys Trp Asn Gly Gln Gly Ala Cys Arg Thr Phe Cys Thr Arg  
   1                                  5                                  10                                  15

Gln Glu Thr Phe Met His Leu Cys Pro Asp Ala Ser Leu Cys Cys Leu  
                   20                                  25                                  30

Ser

<210> 51  
 <211> 33  
 <212> PRT  
 <213> Homo sapiens

<400> 51  
 Gln Arg Cys Trp Asn Leu Tyr Gly Lys Cys Arg Tyr Arg Cys Ser Lys  
   1                                  5                                  10                                  15

Lys Glu Arg Val Tyr Val Tyr Cys Ile Asn Asn Lys Met Cys Cys Val  
                   20                                  25                                  30

Lys

<210> 52  
 <211> 33  
 <212> PRT  
 <213> Mus musculus

&lt;400&gt; 52

Gln Lys Cys Trp Asn Leu His Gly Lys Cys Arg His Arg Cys Ser Arg  
 1 5 10 15

Lys Glu Ser Val Tyr Val Tyr Cys Thr Asn Gly Lys Met Cys Cys Val  
 20 25 30

Lys

&lt;210&gt; 53

&lt;211&gt; 33

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 53

Glu Arg Cys Trp Lys Ser Phe Gly Val Cys Arg Glu Glu Cys Ala Lys  
 1 5 10 15

Lys Glu Ser Phe Tyr Ile Phe Cys Trp Asn Gly Lys Leu Cys Cys Val  
 20 25 30

Lys

&lt;210&gt; 54

&lt;211&gt; 33

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 54

Glu Thr Cys Trp Asn Phe Arg Gly Ser Cys Arg Asp Glu Cys Leu Lys  
 1 5 10 15

Asn Glu Arg Val Tyr Val Phe Cys Val Ser Gly Lys Leu Cys Cys Leu  
 20 25 30

Lys

&lt;210&gt; 55

&lt;211&gt; 33

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 55

Met Lys Cys Trp Gly Lys Ser Gly Arg Cys Arg Thr Thr Cys Lys Glu  
 1 5 10 15

Ser Glu Val Tyr Tyr Ile Leu Cys Lys Thr Glu Ala Lys Cys Cys Val  
 20 25 30

Asp

&lt;210&gt; 56

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<211> 33  
 <212> PRT  
 <213> Mus musculus

<400> 56  
 Asp Thr Cys Trp Lys Leu Lys Gly Ile Cys Arg Asn Thr Cys Gln Lys  
 1 5 10 15  
 Glu Glu Ile Tyr His Ile Phe Cys Gly Ile Gln Ser Leu Cys Cys Leu  
 20 25 30  
 Glu

<210> 57  
 <211> 34  
 <212> PRT  
 <213> Mus musculus

<400> 57  
 Arg Glu Cys Arg Ile Gly Asn Gly Gln Cys Lys Asn Gln Cys His Glu  
 1 5 10 15  
 Asn Glu Ile Arg Ile Ala Tyr Cys Ile Arg Pro Gly Thr His Cys Cys  
 20 25 30  
 Leu Gln

<210> 58  
 <211> 32  
 <212> PRT  
 <213> Mus musculus

<400> 58  
 Lys Glu Cys Lys Met Arg Arg Gly His Cys Lys Leu Gln Cys Ser Glu  
 1 5 10 15  
 Lys Glu Leu Arg Ile Ser Phe Cys Ile Arg Pro Gly Thr His Cys Cys  
 20 25 30

<210> 59  
 <211> 34  
 <212> PRT  
 <213> Mus musculus

<400> 59  
 Lys Ser Cys Thr Ala Ile Gly Gly Arg Cys Lys Asn Gln Cys Asp Asp  
 1 5 10 15  
 Ser Glu Phe Arg Ile Ser Tyr Cys Ala Arg Pro Thr Thr His Cys Cys  
 20 25 30  
 Val Thr

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<210> 60  
 <211> 34  
 <212> PRT  
 <213> Mus musculus

<400> 60  
 Asp Arg Cys Thr Lys Arg Tyr Gly Arg Cys Lys Arg Asp Cys Leu Glu  
   1                  5                  10                  15  
 Ser Glu Lys Gln Ile Asp Ile Cys Ser Leu Pro Arg Lys Ile Cys Cys  
                   20                  25                  30  
 Thr Glu

<210> 61  
 <211> 34  
 <212> PRT  
 <213> Mus musculus

<400> 61  
 Val Asp Cys Arg Arg Ser Glu Gly Phe Cys Gln Glu Tyr Cys Asn Tyr  
   1                  5                  10                  15  
 Met Glu Thr Gln Val Gly Tyr Cys Ser Lys Lys Lys Asp Ala Cys Cys  
                   20                  25                  30  
 Leu His

<210> 62  
 <211> 34  
 <212> PRT  
 <213> Mus musculus

<400> 62  
 Val Asn Cys Lys Lys Ser Glu Gly Gln Cys Gln Glu Tyr Cys Asn Phe  
   1                  5                  10                  15  
 Met Glu Thr Gln Val Gly Tyr Cys Ser Lys Lys Lys Glu Pro Cys Cys  
                   20                  25                  30  
 Leu His

<210> 63  
 <211> 33  
 <212> PRT  
 <213> Mus musculus

<400> 63  
 Glu Arg Cys Glu Lys Val Arg Gly Ile Cys Lys Thr Phe Cys Asp Asp  
   1                  5                  10                  15

Val Glu Tyr Asp Tyr Gly Tyr Cys Ile Lys Trp Arg Ser Gln Cys Cys  
                   20                  25                  30

Val

<210> 64  
 <211> 33  
 <212> PRT  
 <213> Mus musculus

<400> 64  
 Glu Arg Cys Glu Lys Val Arg Gly Met Cys Lys Thr Val Cys Asp Ile  
   1                  5                  10                  15

Asp Glu Tyr Asp Tyr Gly Tyr Cys Ile Arg Trp Arg Asn Gln Cys Cys  
                   20                  25                  30

Ile

<210> 65  
 <211> 33  
 <212> PRT  
 <213> Mus musculus

<400> 65  
 Lys Arg Glu Cys Gln Leu Val Arg Gly Ala Cys Lys Pro Glu Cys Asn  
   1                  5                  10                  15

Ser Trp Glu Tyr Val Tyr Tyr Tyr Cys Asn Val Asn Pro Cys Cys Ala  
                   20                  25                  30

Val

<210> 66  
 <211> 32  
 <212> PRT  
 <213> Mus musculus

<400> 66  
 His Lys Cys Ser Leu Val Arg Gly Thr Cys Lys Ser Glu Cys Asn Ser  
   1                  5                  10                  15

Trp Glu Tyr Lys Tyr Asn Tyr Cys His Thr Glu Pro Cys Cys Val Val  
                   20                  25                  30

<210> 67  
 <211> 33  
 <212> PRT  
 <213> Mus musculus

&lt;400&gt; 67

Glu Thr Cys Arg Leu Gly Arg Gly Lys Cys Arg Arg Thr Cys Ile Glu  
 1 5 10 15

Ser Glu Lys Ile Ala Gly Trp Cys Lys Leu Asn Phe Phe Cys Cys Arg  
 20 25 30

Glu

&lt;210&gt; 68

&lt;211&gt; 33

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 68

Glu Thr Cys Arg Leu Gly Arg Gly Lys Cys Arg Arg Ala Cys Ile Glu  
 1 5 10 15

Ser Glu Lys Ile Val Gly Trp Cys Lys Leu Asn Phe Phe Cys Cys Arg  
 20 25 30

Glu

&lt;210&gt; 69

&lt;211&gt; 33

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 69

Glu Ser Cys Lys Leu Gly Arg Gly Lys Cys Arg Lys Glu Cys Leu Glu  
 1 5 10 15

Asn Glu Lys Pro Asp Gly Asn Cys Arg Leu Asn Phe Leu Cys Cys Arg  
 20 25 30

Gln

&lt;210&gt; 70

&lt;211&gt; 50

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 70

Thr Asn Cys Phe Leu Tyr Leu Ala Arg Thr Ala Ile His Arg Ala Leu  
 1 5 10 15

Ile Ser Lys Arg Met Glu Gly His Cys Glu Ala Glu Cys Leu Thr Phe  
 20 25 30

Glu Val Lys Ile Gly Gly Cys Arg Ala Glu Leu Ala Pro Phe Cys Cys  
 35 40 45

Lys Asn  
 50

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<210> 71  
 <211> 33  
 <212> PRT  
 <213> Mus musculus

<400> 71  
 Phe Leu Cys Lys Lys Met Asn Gly Gln Cys Glu Ala Glu Cys Phe Thr  
 1 5 10 15  
 Phe Glu Gln Lys Ile Gly Thr Cys Gln Ala Asn Phe Leu Cys Cys Arg  
 20 25 30

Lys

<210> 72  
 <211> 33  
 <212> PRT  
 <213> Mus musculus

<400> 72  
 Glu Lys Cys Ser Arg Val Asn Gly Arg Cys Thr Ala Ser Cys Leu Lys  
 1 5 10 15  
 Asn Glu Glu Leu Val Ala Leu Cys Gln Lys Asn Leu Lys Cys Cys Val  
 20 25 30

Thr

<210> 73  
 <211> 33  
 <212> PRT  
 <213> Mus musculus

<400> 73  
 Glu Lys Cys Ser Arg Ile Asn Gly Arg Cys Thr Ala Ser Cys Leu Lys  
 1 5 10 15  
 Asn Glu Glu Leu Val Ala Leu Cys Trp Lys Asn Leu Lys Cys Cys Val  
 20 25 30

Thr

<210> 74  
 <211> 33  
 <212> PRT  
 <213> Mus musculus

<400> 74  
 Glu Lys Cys Asn Lys Leu Lys Gly Thr Cys Lys Asn Asn Cys Gly Lys  
 1 5 10 15  
 Asn Glu Glu Leu Ile Ala Leu Cys Gln Lys Ser Leu Lys Cys Cys Arg

25211793.1

20

25

30

Thr

&lt;210&gt; 75

&lt;211&gt; 33

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 75

Glu Ile Cys Glu Arg Pro Asn Gly Ser Cys Arg Asp Phe Cys Leu Glu  
 1 5 10 15

Thr Glu Ile His Val Gly Arg Cys Leu Asn Ser Arg Pro Cys Cys Leu  
 20 25 30

Pro

&lt;210&gt; 76

&lt;211&gt; 33

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 76

Lys Leu Cys Leu Asp Gln Lys Asp Thr Cys Pro Asp Ser Arg Thr Cys  
 1 5 10 15

Leu Glu Gly Thr Gln Pro Cys His Pro His His Pro Asn Cys Cys Glu  
 20 25 30

Ser

&lt;210&gt; 77

&lt;211&gt; 35

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 77

Arg Pro Cys Glu Lys Met Gly Gly Ile Cys Lys Ser Gln Lys Thr His  
 1 5 10 15

Gly Cys Ser Ile Leu Pro Ala Glu Cys Lys Ser Arg Tyr Lys His Cys  
 20 25 30

Cys Arg Leu  
 35

&lt;210&gt; 78

&lt;211&gt; 33

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 78

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Cys Arg Ser Trp Gly Thr Cys Ser Ile Ala Ala Ile Cys Phe Asp Ser  
 1 5 10 15

Leu Ser Arg Arg Gly Gln Cys Gly Pro Val Lys Asp Pro Cys Cys Pro  
 20 25 30

Leu

<210> 79

<211> 33

<212> PRT

<213> Mus musculus

<400> 79

Cys Arg Ser Trp Gly Thr Cys Ser Ile Ala Ala Ile Cys Phe Asp Ser  
 1 5 10 15

Leu Ser Arg Arg Gly Gln Cys Gly Pro Val Lys Asp Pro Cys Cys Pro  
 20 25 30

Leu

<210> 80

<211> 33

<212> PRT

<213> Mus musculus

<400> 80

Leu Thr Cys Ile Ala Asn Arg Gly Phe Cys Trp His Ser Cys Ile Gln  
 1 5 10 15

Gly Phe Gln Leu Ala Gly His Cys Gly His Pro Lys Val Arg Leu Leu  
 20 25 30

His

<210> 81

<211> 34

<212> PRT

<213> Mus musculus

<400> 81

Leu Val Cys Arg Arg Lys Gly Gly Arg Cys Tyr Ile Lys Cys Pro Asp  
 1 5 10 15

Asn Thr Asp Glx Ile Gly Met Cys Arg Leu Pro Phe Lys Cys Cys Lys  
 20 25 30

Arg Gln

<210> 82

<211> 34

25211793.1

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 82

Leu Ser Cys Trp Met Lys Glx Gly Ile Cys Gln Tyr Arg Cys Phe Gly  
1 5 10 15

Asn Thr His Lys Ile Gly Ser Cys Gly Ala Pro Phe Leu Lys Cys Cys  
20 25 30

Lys Arg

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